Development of selective bispecific Wnt mimetics for bone loss and repair.

Journal: Nat Commun

Publication Year: 2021

Authors: Tristan W Fowler, Troy L Mitchell, Claudia Y Janda, Liqin Xie, Shengjiang Tu, Hui Chen, Haili Zhang, Jingjing Ye, Brian Ouyang, Tom Z Yuan, Sung-Jin Lee, Maureen Newman, Nikita Tripuraneni, Erica S Rego, Devin Mutha, Archana Dilip, Meghah Vuppalapaty, Helene Baribault, Wen-Chen Yeh, Yang Li

PubMed link: 34059688

Funding Grants: San Jose State University Stem Cell Internships for Laboratory-based Learning (SJSU SCILL)

Public Summary:
The Wnt signaling pathway is intricately connected with bone mass regulation in humans and rodent models. We designed an antibody-based platform that generates potent and selective Wnt mimetics. Using this platform, we engineer bi-specific Wnt mimetics that target Frizzled and low-density lipoprotein receptor-related proteins and evaluate their effects on bone accrual in murine models. These synthetic Wnt agonists induce rapid and robust bone building effects, and correct bone mass deficiency and bone defects in various disease models, including osteoporosis, aging, and long bone fracture. Furthermore, when these Wnt agonists are combined with antiresorptive bisphosphonates or anti-sclerostin antibody therapies, additional bone accrual/maintenance effects are observed compared to monotherapy, which could benefit individuals with severe and/or acute bone-building deficiencies. Our data support the continued development of Wnt mimetics for the treatment of diseases of low bone mineral density, including osteoporosis.

Scientific Abstract:
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